Current CDER Initiatives

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Disclosure Statement

I have no financial relationships with proprietary entities that produce health care goods and services

The opinions and information in this presentation are my own and do not necessarily reflect the views and policies of the FDA

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Drivers for CDER Priorities

- Diverse stakeholders and expectations
- Statutory requirements: FDAAA, FDASIA, Sunscreen Innovation Act, Appropriations Bill
- User Fees: PDUFA, GDUFA, BSUFA
- All tied to CDER mission to protect and promote human health by ensuring that safe and effective drugs are available to Americans

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FDA Challenge

- **Patients and Caregivers want**:
  - Rapid access to safe and effective new drugs made with reliable quality
  - Better information about how to use these drugs after approval
- **Inefficient medical product development**:
  - Is failing to keep pace with the new scientific discoveries
  - Is delaying access to new innovations and limit information on appropriate use of approved drugs

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Scope of Work

- In addition to these priority initiatives and other initiatives--
- Tens of thousands of decisions made yearly
  - Application-specific: IND, NDA, Supplement
  - Thousands of meetings with industry
  - FOI requests
  - Citizen Petitions
  - Advisory Committees
  - Compliance decisions (imports, inspections)
  - Communications
  - Safety Evaluations for marketed drugs

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CDER Response to Challenges: Focus and Prioritization within our Public Health Mission

CDER Major Priorities

- Generic Drugs
  - GDUFA Implementation
  - Continue to build Office of Generic Drugs
- Compounding
- Pharmaceutical Quality
  - Stand up Office of Pharmaceutical Quality
  - Program Alignment Group (PAG) activities with ORA
  - Continued work on international activities

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Foundation: People and Infrastructure

- New IT System to integrate data systems across CDER
  - Replace current application archiving system ("DAARTS")
  - Pharmaceutical Platform to integrate quality review work
  - Office of Generic Drugs Data system up and helping address generics goals
- People
  - ~4200 CDER employees, varied skills
  - New senior leadership

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Generic Drugs

- Standing up Office of Generic Drugs
- GDUFA Goals
- Dialogue

Standup of OGD “Super-Office”

- Re-organization carefully planned to support critical functions of generic drug review
- Several key leadership positions filled
- Over 200 new hires last year in positions focused on product review
- OGD business being managed in new IT system
- Working through administrative roadblocks to generic approval via “Drug Lifecycle Council”

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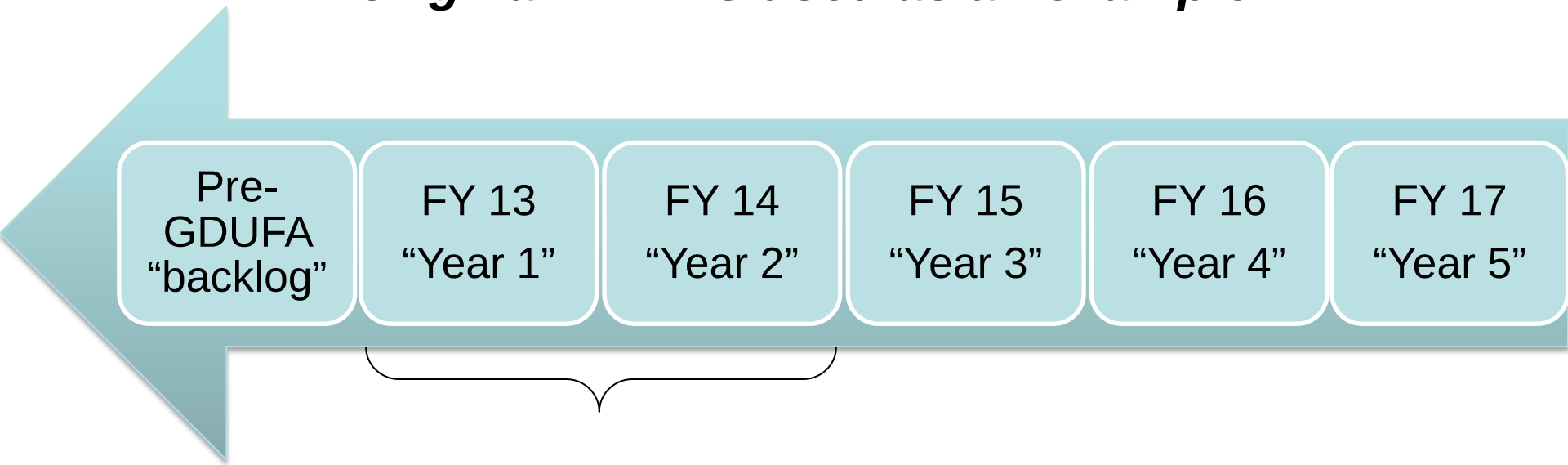
GDUFA Submission Cohorts & Goals

Original ANDAs used as an example



- Take action on 90% by end of Year 5
- Expedite review of PIV
- Maintain productivity to extent possible given hiring, training, program and system development activity
- Take action on 60% within 15 months of submission
- Take action on 75% within 15 months of submission
- Take action on 90% within 10 months of submission

Ongoing Work

- Filing Backlog
  - Priority applications will be expedited
  - Typical assessment time for filings
    - Current/GDUFA Year 3 submissions: 27 days
- Controlled Correspondence:
  - Year 3: 70% within 4 months (exceeding)
  - Year 4: 70% within 2 months
  - Year 5: 90% within 2 months
  - Extra month for clinical issues
- Application Backlog: progress is being made

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Suggestions to Speed Actions

- Check-list:
  - http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/UCM320405.pdf
- Guidance on Refuse-to-Receive Standards:
  - http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM370352.pdf
- Electronic format:
  - Highly recommended (for GDUFA Goals)
- Quality matters:
  - Complete submissions, facilities ready for inspection

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Dialogue: Public Meetings

- FY 2015 Regulatory Science Initiatives - June 5, 2015
  - Overview of regulatory science initiatives.
  - Opportunity for public input on research priorities.
  - http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/ucm436485.htm
  - Watch for future meetings.

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Dialogue: Public Meetings

- GDUFA II June 15, 2015
  - Seeking participation (i.e., attendance and oral presentations)
  - If you wish to attend the meeting, please email your registration information to GenericDrugPolicy@fda.hhs.gov by June 1, 2015.

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Compounding

- Implementing “Compounding Quality Act” of the Drug Quality and Security Act (DQSA)
  - Outsourcing Facilities under Section 503B
- Inspections
- Guidances
- Other Actions

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Compounding Quality Act

- Removes certain provisions from section 503A related to solicitation of prescriptions and advertising and promotion that were found to be unconstitutional by the U.S. Supreme Court in 2002
- Clarifies that section 503A is applicable to compounders nationwide
- Adds new section 503B:
  - Defines “Outsourcing Facilities” and impact of being designated one

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Outsourcing Facility Implementation

- Established registration and reporting mechanisms
- Established fee program, including small business reduction
- As of March 31, 2015, 51 facilities were registered as outsourcing facilities

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Inspections and Resulting Actions

- Since enactment of the DQSA, FDA has:
  - Conducted approximately 140 inspections of compounders including approximately 40 inspections of compounders registered as outsourcing facilities
  - Approximately 45 of the 140 inspections of compounding facilities since enactment of the DQSA have been for-cause, generally based on reports of serious adverse events or product quality issues such as drug contamination

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Inspections and Resulting Actions

Also since enactment of the DQSA, FDA has:

- Overseen recalls by over 20 compounders
- Issued over 40 warning letters
- Issued about 10 State referral letters
- Obtained 2 consent decrees
- Obtained 3 criminal prosecutions, including one guilty plea and 2 indictments

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Guidances Issued Since DQSA

- Draft and Final Guidances:
  - 503A
  - Outsourcing Facility Fees
  - Registration of Outsourcing Facilities
- Draft Guidances:
  - Interim CGMP for Outsourcing Facilities
  - Guidance For Entities Considering Whether to Register as Outsourcing Facilities
  - Adverse Event Reporting for Outsourcing Facilities
  - Draft and Revised Draft Product Reporting Guidances for Outsourcing Facilities
  - Repackaging
  - Mixing, Diluting, and Repackaging Biologics

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Other Actions

- Issued draft Standard Memorandum of Understanding (MOU) under 503A between FDA and States
- Issued proposed rule describing additions and modifications to the Withdrawn or Removed List (503A and 503B)
- Solicited nominations for 503A and 503B bulks lists and for drugs that are difficult to compound under sections 503A and 503B
- Announced membership of Pharmacy Compounding Advisory Committee and held first meeting covering drugs proposed for withdrawn or removed list and 503A bulks list
- Held three 50-State meetings
- Met with Federal partners
- Conducted listening sessions with over 40 other stakeholders

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Pharmaceutical Quality

- Stand up Office of Pharmaceutical Quality
- Program Alignment Group (PAG) activities with ORA
  - Continued work on international activities
- Continuous Manufacturing

Standup of Office of Pharmaceutical Quality

- Follows two years of planning and discussion
- Centralizes quality review for new and generic drugs
  - New and lifecycle drug product offices
  - Office of Process and Facilities with microbiology, process, and facility inspection divisions
  - Office of Surveillance for post-market inspections and surveillance in conjunction with ORA
  - Centralized project management—largest throughput office in Center
  - Policy and Research Offices

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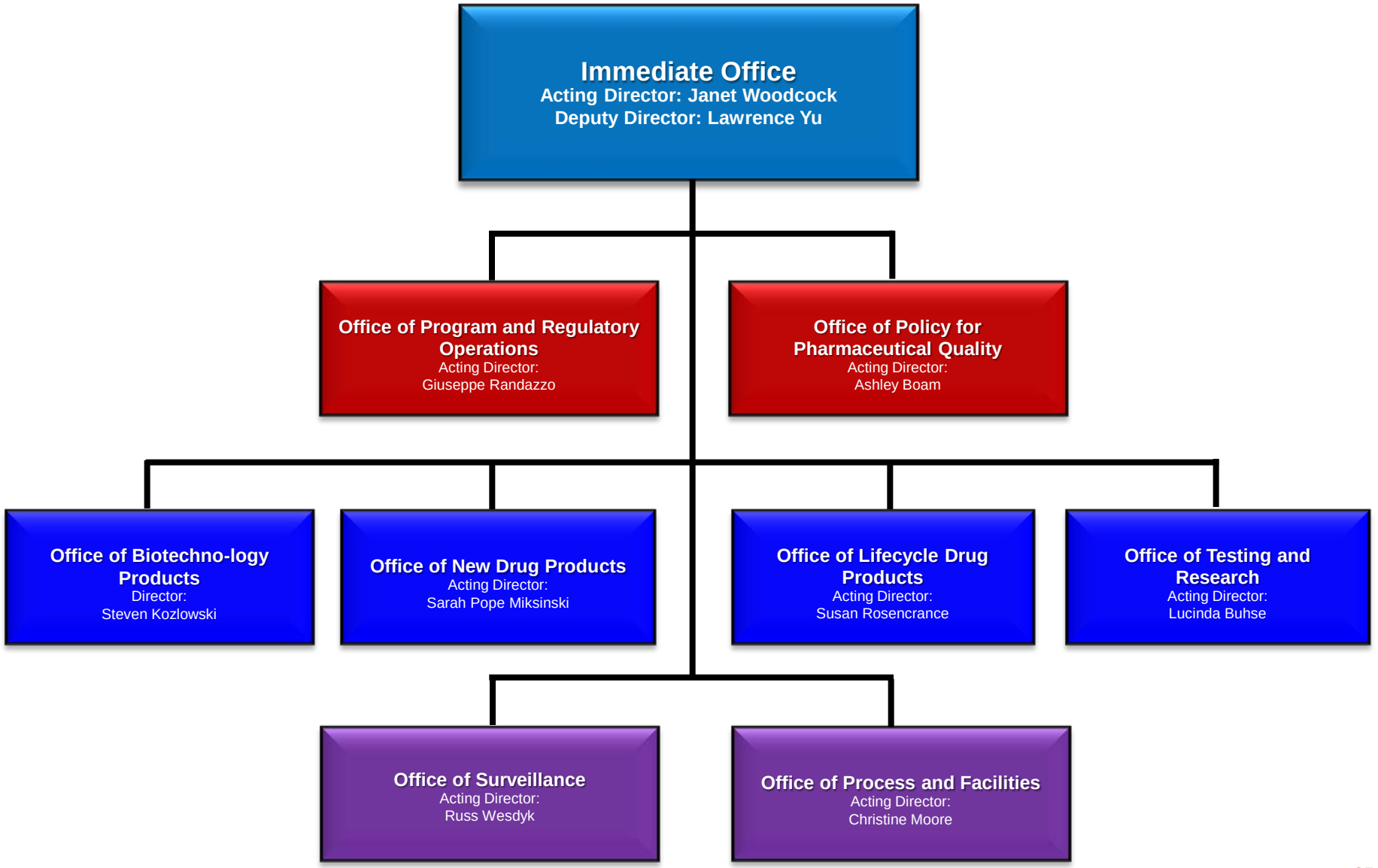
Office of Pharmaceutical Quality



OPQ: New Surveillance Function

- Seeks to identify quality status of all facilities manufacturing drugs for US market
  - Integrate intelligence from many sources: applications, inspections, “quality metrics”
  - Aided by new quantitative template for inspections being developed by ORA and CDER—scoring system to include “exceeding” minimal expectations as well as not meeting. Risk based.
- Surveillance Office will integrate all the info in a risk model to target inspections

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OPQ Objectives

- Product Quality Platform (IT) to support lifecycle management
- Quality Metrics and FDA lab-based surveillance
- Comprehensive Quality Overall Summary/Structure-based Review
  - Same quality standard for new and generic drugs
- Project on a New Inspections Protocol

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New Surveillance Function: Quality Metrics

- Intend to collect well-understood metrics from facilities regarding state of quality
- Metrics widely used in quality management in most large-scale manufacturing sectors
- Will take time to understand and integrate into life-cycle

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Challenge of Globalization

- Global focus on quality
  - Shared goal internationally
  - Risk-based enforcement
  - Carrots and sticks
- Cooperation between international regulators to enhance information-sharing
- Need for dedicated expertise aligned to specific products
  - Process Alignment Group (PAG) activities between Centers and inspectorate (ORA)

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CDER-ORA PAG Agreement

- Integrate ORA facility pre-approval inspections into OPQ team review
- Specialized pharmaceutical inspectorate in ORA will work closely with CDER
- Share data from various systems seamlessly
- Pilots ongoing, templates under development

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Other CDER Priorities: Product Development

- Biosimilars
  - Zarxio approval (biosimilar to Neupogen)
    - Biologics Price Competition and Innovation Act (2009)
  - Guidance on how current and future biological products marketed in the US should be named
- Antibiotic and anti-viral development
- Review of Breakthrough Designations process

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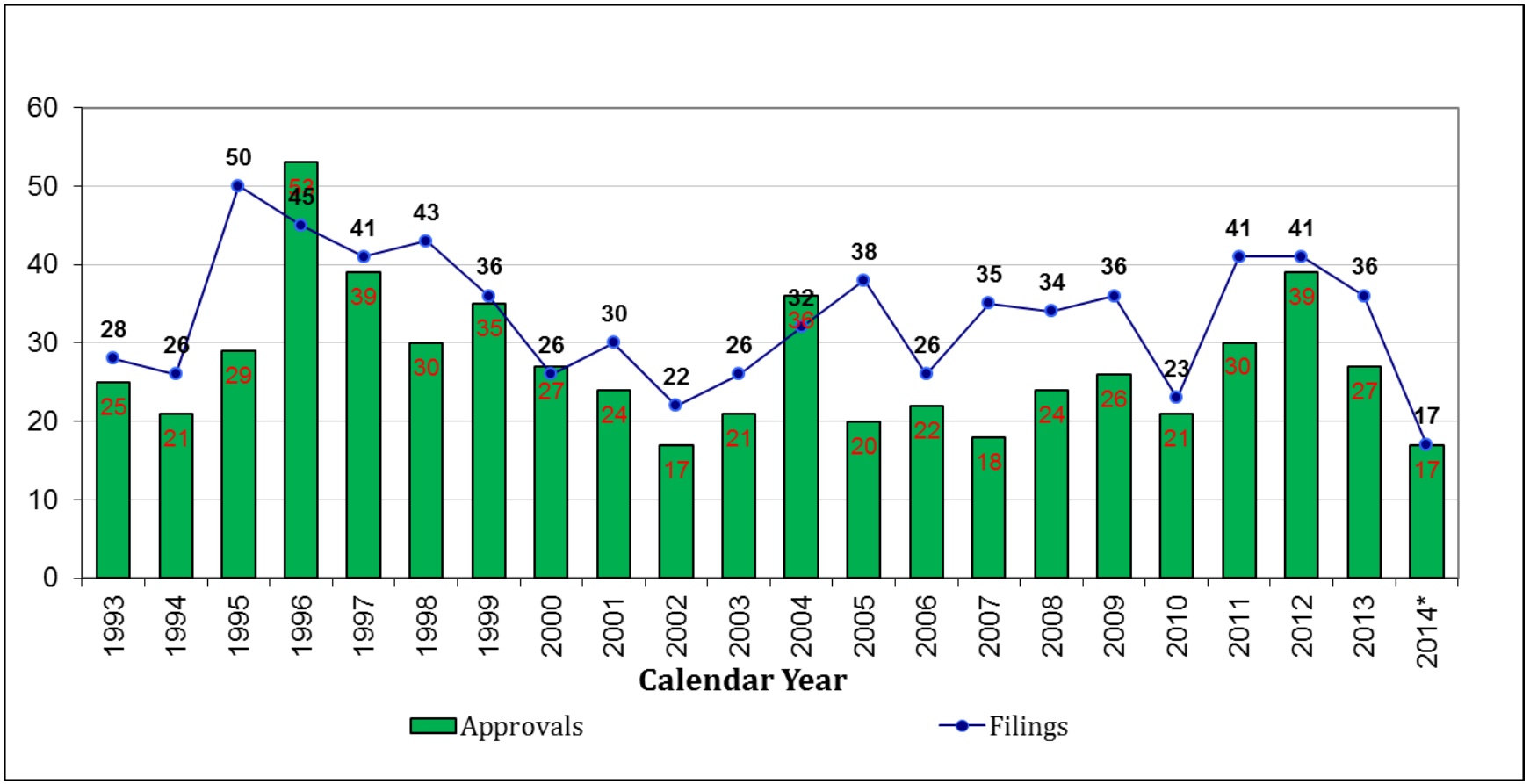
Other CDER Priorities: Product Development (cont)

- Review of Expanded Access program
- 21st Century Cures–
  - working to advance medical products that are valuable for patients and public health

CDER NME NDAs/BLAs† Filings and Approvals



Data as of 6/30/2014

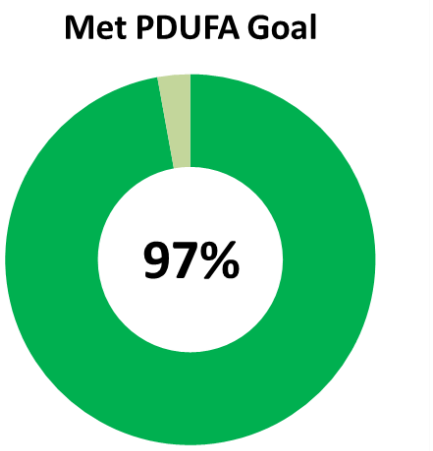
† Multiple applications pertaining to a single new molecular/biologic entity (e.g. single ingredient and combinations) are only counted once. Therefore, the numbers represented here for CY14 filings are not indicative of workload in the PDUFA V Program.

† Original BLAs that do not contain a new active ingredient are excluded

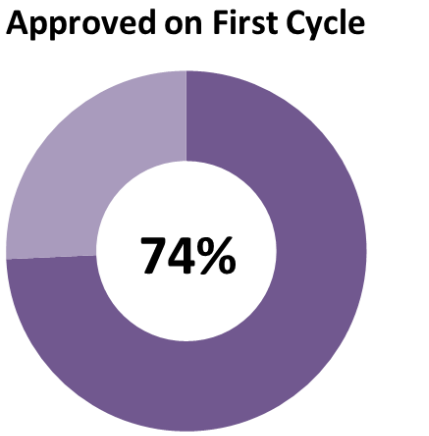
*Since applications are received and filed throughout a calendar year, the filed applications in a given calendar year do not necessarily correspond to an approval in the same calendar year. Certain applications are within their 60-day filing review period and may not be filed upon completion of the review.

In CY 2014, CDER Continued To Ensure The Efficiency Of First Cycle Review

- All but one of the novel drugs approved to date in CY14 met their PDUFA goal dates for the approval review cycle



- Almost three-quarters (74%) of the novel drugs, approved to date in CY14, were approved in the first review cycle



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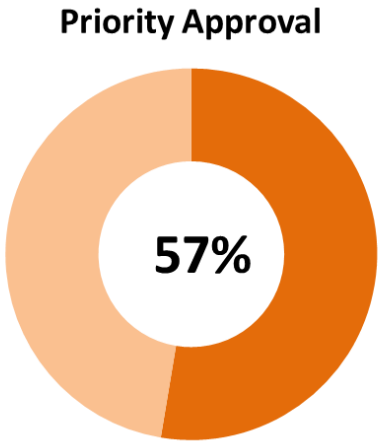
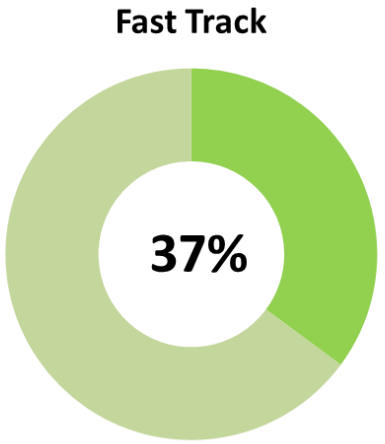
CDER Ensures That Novel Drugs Receive Expedited Review

- More than half (57%) of the novel drugs approved to date in CY14 were approved under Priority Review



- More than one-third (37%) of novel drugs approved to date in CY14 received Fast Track designation



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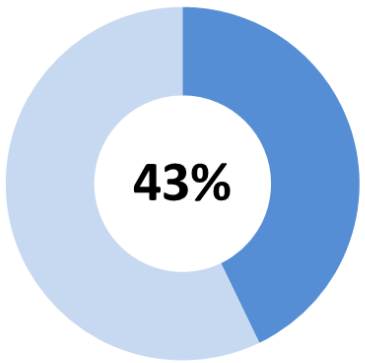
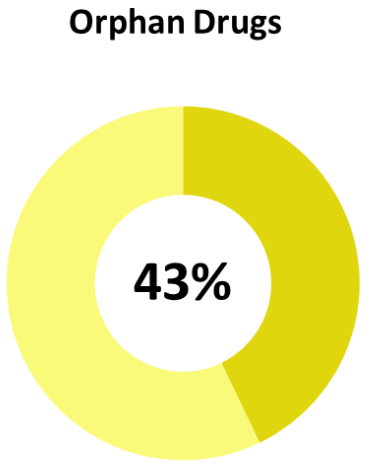
2014 Continues A Strong Track Record For Drug Innovation

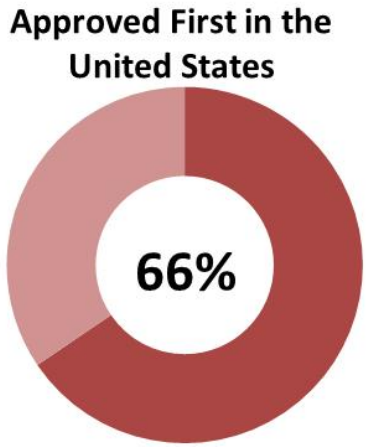
- Four out of every ten (43%) novel drugs approved to date in CY14 are for rare diseases

Four out of every ten (43%) of novel drugs approved to date in CY14 are the first in their class

Two-thirds (66%) of novel drugs approved to date in CY14 were first approved in the U.S.







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Other CDER Priorities: Safety Science

- Sentinel network
  - Augments existing work, doesn't replace it
- Work to address opioids abuse
  - Abuse deterrent formulations of opioids
- Standardizing and evaluating REMS
  - Work on 4 priority projects from 2014 report
- Building pharmacoepidemiology expertise
  - Importance of assessing specific product use after approval-- opioids
  - IMEDS will help with thisa

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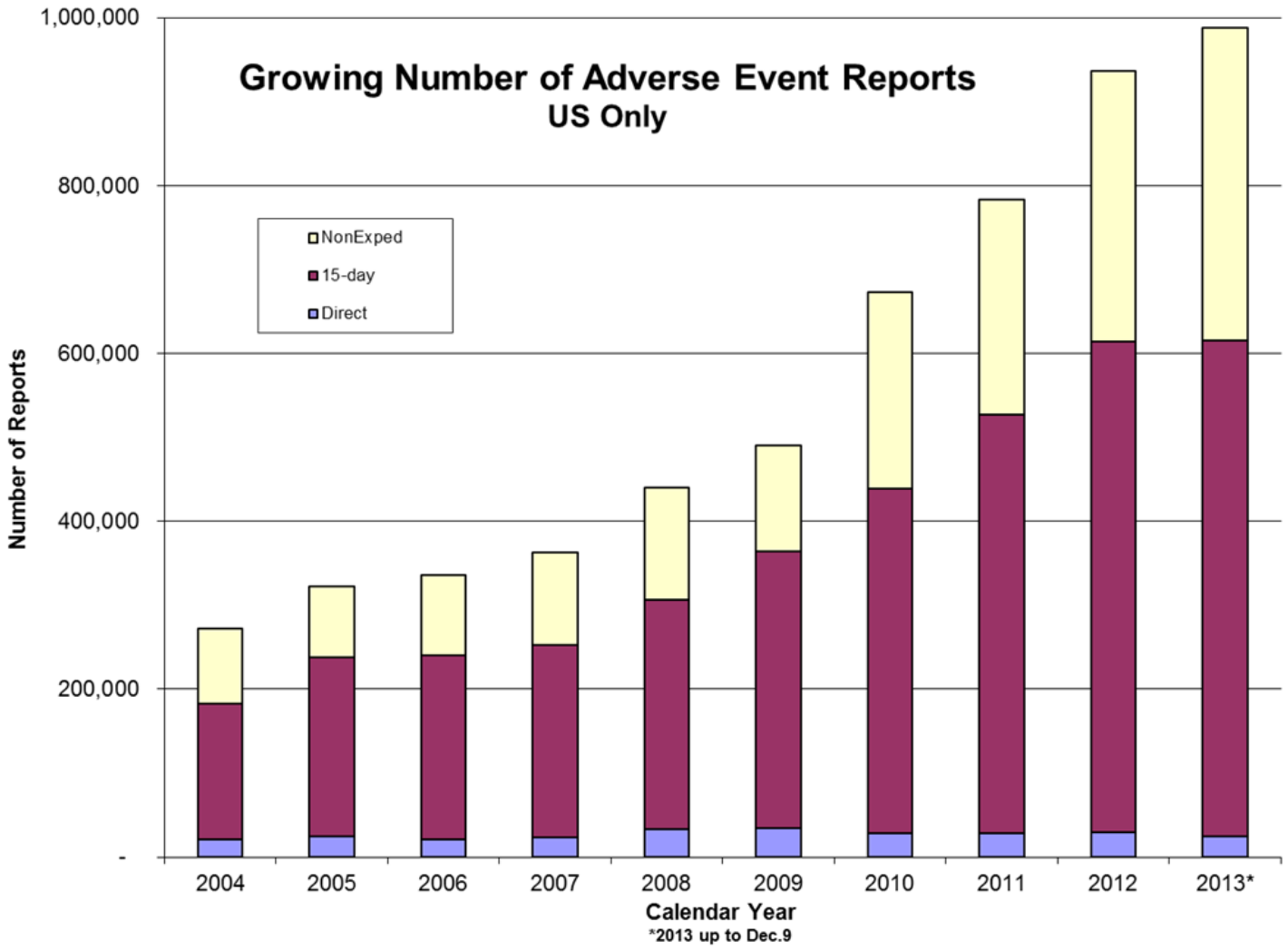
Continued Growth in Adverse Events Reported to FDA



Mini-Sentinel – Transition to Sentinel

- Awarded to Harvard Pilgrim Healthcare Institute
- 50+ healthcare and academic organizations
- Will build on existing infrastructure and capabilities
  1) Summary tables – precalculated tables
  2) Modular SAS programs – reusable, similar to SAS Procs
  3) Protocol based assessments - custom SAS programs for in-depth assessments
  4) PROMPT

Harvard Pilgrim Health Care

newsrelease

For Immediate Release
October 1, 2014

Contact: Mary Wallan
(617) 509-2419
mary_wallan@hphc.org

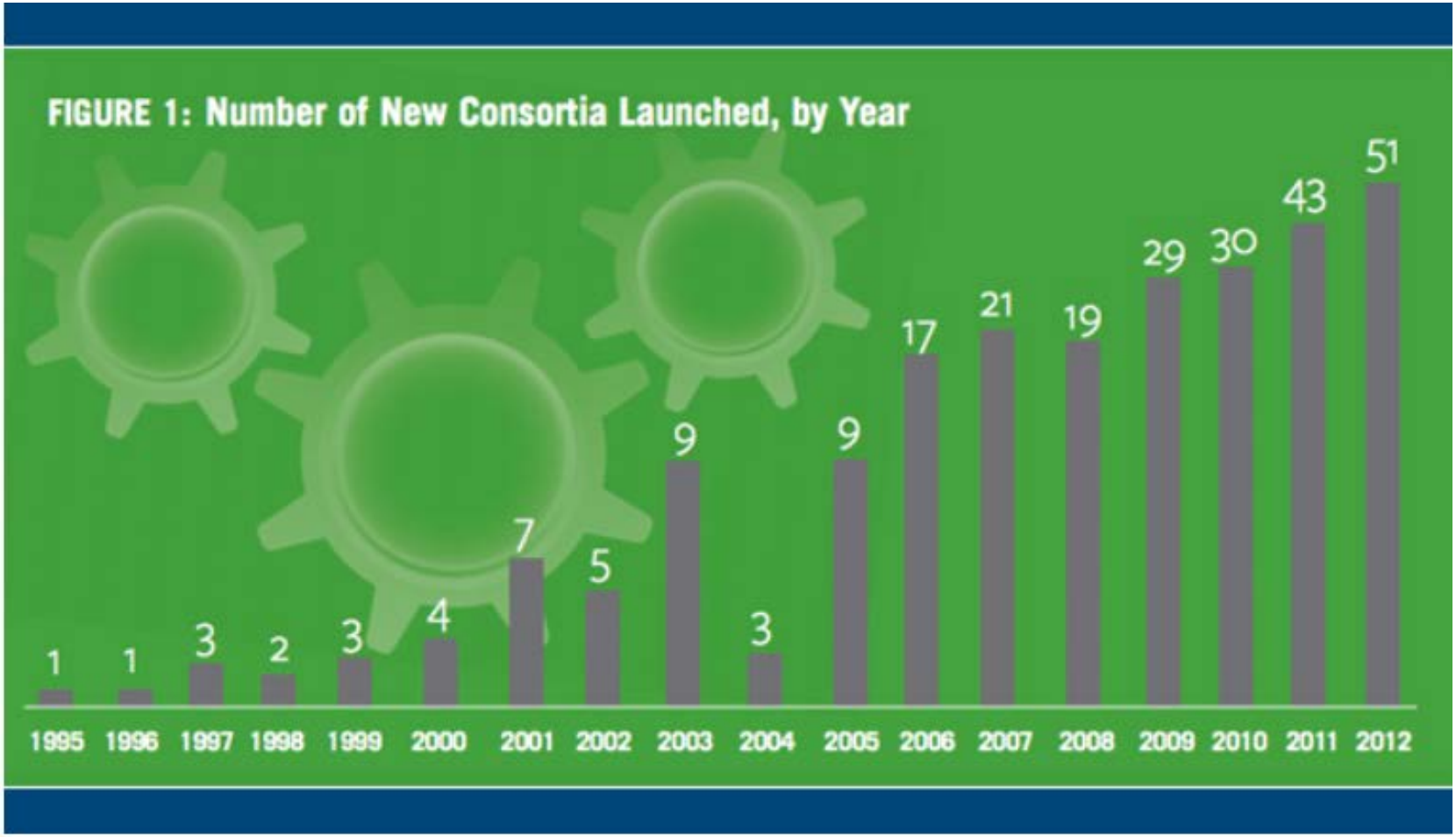
FDA awards $150 million Sentinel contract to Harvard Pilgrim Health Care Institute

(Boston, MA) The U.S. Food and Drug Administration (FDA) has awarded a contract for up to $150 million to Harvard Pilgrim Health Care Institute to lead the Sentinel System, a program using electronic healthcare data to monitor the safety of FDA-regulated drugs and other medical products. The Institute will partner with over 50 health care and academic organizations across the nation on this important undertaking.

Other CDER Priorities: Regulatory Science

- Advancing Regulatory Science and Expediting Drug Development
  - Combination products
    - Cross-Agency coordination
  - Advancing Regulatory Science
    - Consortial model of scientific advance
    - Methods for regulatory meta-analysis
    - Biomarkers and patient-reported outcomes
    - Pharmacogenomics and support for personalized medicine
    - Novel trial designs to help speed drug testing
  - Development of drugs for rare diseases

Use of Consortia To Support Efficient Drug Development



http://consortiapedia.fastercures.org/

Critical Path Innovation Meetings (CPIMs)

- New program
- Opportunity for dialogue on challenges in drug development
  - Novel clinical trial designs and challenging areas of development
  - Potential biomarkers before qualification
  - Natural history studies
  - Intended as dialogue, not for formal regulatory advice about product specific development

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http://www.fda.gov/drugs/developmentapprovalprocess/druginnovation/ucm395888.htm

Other CDER Priorities: Communications

- Internal communications
  - Benefit-Risk Framework
    - To be applied to all NMEs and original BLAs
    - Link to Patient Focused Drug Development meetings
- External Communications
  - Drug Snapshots
  - CDER publications
- External Collaborations
  - Patient Focused Drug Development meetings
  - Professional Affairs and Stakeholder Engagement (PASE)

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Office of Communications

- New OCOMM Office Director – Chris Shreeve
- Expanded Publication Efforts Related to FDA Work
  - 16 op-ed/perspective articles for peer-reviewed scientific publications
- Expanded Presence on Digital & Social Media
  - Mobile App for Drug shortage launch
  - More apps in development- Orange book & Drugs at FDA *lite*
  - Expanded reach on social media platforms (Twitter & Facebook)
- Expanded Collaborations
  - Partnered with 3 major educational campaigns with Partnership for Drugfree, NCPIE, & National Consumers League

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Drug Snapshots

- Responsive to concerns about participation in drug trials (FDASIA Section 907)
- Provide Information to the public about
  - Who participated in the clinical trials
  - Study design, results of studies
  - Were there any differences seen in how well the drug worked in clinical trials or in side effects seen among sex, race, and age?
  - Not product labeling

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Drug Trials Snapshot Publication

- In November 2014, first snapshots were published
  - 6 indications for 5 NMEs
  - Covered 2-month period in 2014
  - Public Comment Period after publication
- Going forward, FDA publishing snapshots for all approved NMEs and original biologics

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Continuing Priorities: Emergency Preparedness

- Response to Ebola
  - Coordination with USG to speed response
- Ongoing work to prevent or mitigate critical drug shortages
  - Report to Congress
- Medical Countermeasures development
- Prescription opioids abuse
  - Guidance on Abuse-Deterrent Opioids

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Continuing Priorities

- Ongoing priority activities that continue to perform well:
  - PDUFA process
    - New drug development
    - Implementation of 21st Century Review
  - FOI :
    - Reducing the backlog in the face of a higher request rate
  - Advisors and Consultants
    - Continued interest in, and need for public advisory committee meetings

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Summary

- CDER continues to work on multiple priority initiatives
  - Focus on drug use throughout product life-cycle for both innovators and generics
  - Focus on anticipating trends and needs
  - Capable of rapid response to public health crisis
- Work involves management, implementation of statutory requirements, systems improvement, and personnel actions
- In addition to user fees, product quality, and globalization, drug development and drug safety continue as high priorities for CDER

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Conclusions

- This is a transformational time in the healthcare system, including drug regulation
  - Expectations, resources, and challenges are all changing
- CDER is confronting these changes, while remaining true to our historic mission and statutory framework
- Success will require discipline, creativity, a willingness to question assumptions, and a willingness to try new solutions when needed

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- The art of progress is to preserve order amid change and to preserve change amid order

---Alfred North Whitehead

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Ongoing Work

Applications	Review and Act On:
Backlog (pending on Oct 1, 2012)	**90% by the end of FY 2017 (Sep 30, 2017)**

- GDUFA Year 1 and 2 applications:
  - Incorporated into the ANDA work plan
  - Priority applications will be expedited
  - Progress on eliminating backlog is being made

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